UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,379	08/02/2006	Tomas J. Ekstrom	2836-0163PUS1	8424

2292 7590 04/23/2010

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
EPPS -SMITH, JANET L	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
04/23/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/588,379	EKSTROM ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Smith	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02/16/2010 & 0317/2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13-46,58-62 and 64-68* is/are pending in the application.

4a) Of the above claim(s) *2-11,13-20,32-46,58-61 and 64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,21-31,62 and 65-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-11, 13-46, 58-62, and 64-68 are presently pending.

2. Claims 2-11, 13-20, 32-61 and 64 are withdrawn, and SEQ ID NO: 4-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

3. Claims 1, 21-31, 62, and 65-68 are under examination.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Claim Rejections - 35 USC § 102

5. Claims 1 and 62, 65-68 remain rejected under 35 U.S.C. 102(b) as anticipated by Chung et al. (2000).

6. Applicant's arguments filed 02/6/2010 have been fully considered but they are not persuasive. Applicants traversed the instant rejection on the grounds that although "[C]hung et al. links the activation of thymidine kinase to the function of PB and the nucleoside analogue. The thymidine kinase described in Chung is an endogenous kinase and, accordingly, is not a component in a pharmaceutical composition." The instant claims read on "a pharmaceutical composition comprising at least one compound capable of enhancing gap-junction communication, at east one nucleoside analogue *and* a source of deoxyribonucleoside kinase." Contrary to Applicant's assertions, Chung et al. teach a source of deoxyribonucleoside kinase *and* compositions comprising phenylbutyrate and ganciclovir. The instant claims

encompass a pharmaceutical composition that includes a source of deoxyribonucleoside kinase, therefore Chung et al. reads on the claimed invention.

Claim Rejections - 35 USC § 103

7. Claims 1, 21-31, 62, and 65-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over DiMartino in view of Yang et al. and Lavie et al.

8. Applicant's arguments filed 02/6/2010 have been fully considered but they are not persuasive. Applicants traversed the instant rejection on the grounds that the DiMartino reference does not teach or suggest a deoxycytidine kinase that is part of a pharmaceutical composition. Contrary to Applicant's assertions the instant claims read on "a pharmaceutical composition comprising at least one compound capable of enhancing gap-junction communication, at east one nucleoside analogue *and* a source of deoxyribonucleoside kinase." DiMartino clearly teaches a source of deoxyribonucleoside kinase, as evidenced by the conversion of decitabine into its active form by deoxycytidine kinase.

9. Regarding Lavie et al. (US 20070258968A1), Applicants argue that this reference does not teach or suggest the use of the gap junction communication-enhancing compounds. Contrary to Applicant's assertions, this reference is provided for its disclosure of modified deoxycytidine kinase (dCK) mutants with such enhanced activity. Additionally, regarding Yang et al. Applicants argue that Yang does not teach or suggest the use of gap junction communication enhancing compounds or the use of nucleoside analogues.

10. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

11. DiMartino et al. is cited for its disclosure of compositions comprising a combination of a DNA methylation inhibitor (including nucleotide analogs) and an effective amount of a histone deacetylase inhibitor, which includes phenlybutyrate. The specification as filed describes phenlybutyrate as a compound which is capable of enhancing gap-junction communication.

12. Applicants further argued that the claimed pharmaceutical result in effects that could not have been expected by an ordinary artisan at the time of the invention. Specifically, Applicants argued:

"[I]n contrast, the claimed pharmaceutical composition has numerous and unexpected advantages. For example, an exogenously applied kinase may be delivered locally to the desired tumor area only. In addition, the kinase is selected for a specific purpose, and accordingly, a kinase may be selected that has high affinity towards particular nucleoside analogs. Thus, in this aspect, the claimed pharmaceutical composition is far superior to any .endogenous kinase: Further, the addition of 4-PB, surprisingly, enhances the well known bystander effect." This is an effect that is facilitated by gap junctions, which are formed between adjacent cells, allowing small molecules to diffuse freely. Thus, a small, toxic molecule having an effect in one cell can also have an effect in an adjacent cell, i.e., a 'bystanding' cell."

13. Applicant's assertions of superior results are not supported by any factual evidence. Absent evidence to the contrary, the compositions produced by the combination of the cited references would potentially possess the same characteristics

as Applicant's compositions. Additionally, regarding the effects of 4-PB, it is noted that the instant claims are not limited to 4-PB. Thus, the results observed with the use of 4-PB are not commensurate in scope with the instant claims.

14. Claims 1, 21-31, 62, and 65-68 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Murphy et al. in view of Gold et al. and Jian et al.

15. Applicant's arguments filed 02/16/2010 and 03/7/2010 have been fully considered but they are not persuasive. Applicants argue that Murphy and Gold do not teach or suggest the use of gap junction communication enhancing compounds in the treatment of cancer.

16. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

17. As stated in the prior Office Action, Jian et al. teach the combination of adenovirus mediated suicide gene therapy with the histone deacetylase inhibitors butyrate and phenlybutyrate. The specification as filed describes phenlybutyrate as a gap junction communication enhancing compound.

18. Additionally, regarding the effects of 4-PB, it is noted that the instant claims are not limited to 4-PB. Thus, the results observed with the use of 4-PB are not commensurate in scope with the instant claims.

19. In the reply filed 03/17/2010 Applicants assert that the Jian et al. reference does not qualify as prior art under 35 USC 102(b). Contrary to Applicant's assertions, the Jian et al. reference was published in July 2003, which is well before the earliest filing date of February 25, 2004. Jian et al. clearly qualifies as prior art under 102(a), and therefore qualifies as prior art under 103(a).

Claim Rejections - 35 USC § 112

20. The rejection of claims 30-31 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in response to Applicant's amendment to the claims.

Conclusion

21. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Smith whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Smith/
Primary Examiner, Art Unit 1633